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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/037,243	01/04/2002	Paul I. Freimuth	BSA 01-22	6646

26302 7590 10/03/2008
BROOKHAVEN SCIENCE ASSOCIATES/
BROOKHAVEN NATIONAL LABORATORY
BLDG. 185 - P.O. BOX 5000
UPTON, NY 11973

EXAMINER

HIBBERT, CATHERINE S

ART UNIT	PAPER NUMBER
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1636

NOTIFICATION DATE	DELIVERY MODE
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10/03/2008

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

ott@bnl.gov
pacella@bnl.gov
lneiger@bnl.gov

Office Action Summary	Application No.		Applicant(s)	
	10/037,243		FREIMUTH ET AL.	
	Examiner		Art Unit	
	Catherine S. Hibbert		1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 16 May 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 64 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 64 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--------------------------------------------------------------------------------------|-------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 16 May 2008 has been entered.

Please note that the Examiner for this Application has changed. This is a continued examination of US Application 10/037,243, filed 4 January 2002. Claims 1-63 and 65-100 are cancelled. Claim 64 is presently amended and is pending and under examination in this action.

Response to Arguments

The rejections of cancelled Claims 99-100 are moot in view of the cancellation of Claims 99-100.

The rejection of claim 64 under ¶ 112, first paragraph, (written description requirement), has been withdrawn based on Applicant's Amendment to the Claims filed 16 May 2008 and therefore Applicants Arguments are moot.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 64 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "poor solubility" in claim 64 is a relative term which renders the claim indefinite. The term "poor solubility" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. For example, it is indefinite as to the degree of solubility that is encompassed by the word "poor" and therefore one of ordinary skill in the art would not be able to determine the metes and bounds of Applicants invention.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 64 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a rejection for new matter.**

The specification does not describe a pET-15b expression vector comprising a first nucleic acid sequence encoding a peptide extension for enhancing the solubility and proper folding of a protein or polypeptide of interest, wherein the encoded peptide

extension is Peptide T7B (SEQ ID NO: 6), the expression vector further comprising a multiple cloning site for inserting, in-frame with said first nucleic acid sequence, a second nucleic acid sequence encoding said protein or polypeptide of interest, said protein or polypeptide having a carboxyl- and an amino- terminus, wherein expression of the first and second nucleic acid sequences yields a fusion protein consisting of the encoded peptide extension fused to the carboxyl-terminus of the protein or polypeptide of interest, and wherein the protein or polypeptide of interest exhibits poor solubility and/or improper folding when expressed in the absence of fusion to said peptide extension. **The term “poor solubility” in the context of claim 64 is new matter.**

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 64 is rejected under 35 U.S.C. 103(a) as being unpatentable over Freimuth et al in "Coxsackievirus and Adenovirus Receptor Amino-Terminal Immunoglobulin V-Related Domain Binds Adenovirus type 2 and Fiber Knob from Adenovirus Type 12" (Journal of Virology, February, 1999, Vol. 73, No.2, pages 1392-1398; made of record in the IDS), in view of Condrón et al in "Frameshifting in gene 10 of bacteriophage T7" (J Bacteriol 1991, Vol. 173 No. 21, pages 6998-7003; made of record in the IDS and as cited in the Score Report for SEQ ID NO:6, Result 1).

Initially it is noted that the claim reads on a composition and as such the intended use language in the claim that pertains to the terms: "for enhancing the solubility and proper folding of a protein or polypeptide of interest" and

for inserting, in-frame with said first nucleic acid sequence, a second nucleic acid sequence encoding a protein or polypeptide of interest, said protein or polypeptide having a carboxyl- and an amino- terminus, wherein expression of the first and second nucleic acid sequences yields a fusion protein consisting of the encoded peptide extension fused to the carboxyl-terminus of the protein or polypeptide of interest, and wherein the protein or polypeptide of interest exhibits poor solubility and/or improper folding when expressed in the absence of fusion to said peptide extension,

do not bear patentable weight when applying prior art to the claims. Thus, the claims, as written, are interpreted to read on any pET-15b expression vector comprising a first nucleic acid sequence encoding a peptide extension, wherein the encoded peptide extension is Peptide T7B (SEQ ID NO: 6), the expression vector further comprising a multiple cloning site.

Freimuth et al teach a pET-15b expression vector comprising a multiple cloning site and a nucleic acid sequence encoding a peptide extension that increases the solubility of the linked fusion protein (e.g. page 1393, Figure 1(C) and legend; page 1394, ¶¶ bridging left and right column). Freimuth et al teach that the peptide extension contains the 22 amino acid sequence LEDP/AANKARKEAELAAATAEQ. It is noted that the peptide extension of Freimuth et al is the four amino acids LEDP contiguously in sequence with the carboxyl-terminal 18 residues of the phage T7 gene 10B protein.

Freimuth et al differ from the invention claimed in the instant Claim 64 because Freimuth et al fail to teach the peptide extension is the T710B (SEQ ID NO:6). It is noted that SEQ ID NO:6 is a 44 amino acid sequence that begins with the first four amino acids of the peptide extension of Freimuth et al (LEDP) contiguously in sequence with the carboxyl-terminal 40 residues of the phage T7 gene 10B protein.

The Score Report, in light of Condron et al teach the amino acid sequence of the T7 gene 10B protein, including the carboxyl-terminal 40 residues.

Absent evidence to the contrary, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have substituted the 40 amino acid residue sequence for the 18 amino acid residue sequence of the phage T7 gene 10B

protein (see Score Report of SEQ ID NO:6 and Cordon et al) in the pET15b vector containing the 22 peptide extension taught in Freimuth et al because Cordon et al (see SCORE report) teach the 40 amino acid sequence of the carboxyl-terminal 10B protein was known and Freimuth et al proposed using mutagenesis approaches, regarding the 22 amino acid peptide extension study, for the optimization of Ad2 knob solubility. (It is noted that Ad2 knob is a protein of interest tested in the expression vector containing the 22 amino acid peptide extension). Since the 22 amino acid extension consisted of the last 18 amino acids of the 10B gene, it would have been obvious to one of ordinary skill in the art for the “mutagenesis” regarding the solubility peptide extension to include addition of the next contiguous amino acids starting from the last 18 amino acids of the 10B gene, as shown in Applicants invention (page 1397, right column, paragraph 2).

One would have been motivated at the time the invention was made to have extended the peptide extension substituting the longer peptide extension containing the carboxyl-terminal 40 amino acid residues of the phageT7 gene 10B protein because Freimuth et al stated that the solubility of a D1 protein depended on the presence of the 22 amino acid peptide extension (page 1397, left column, paragraph 4) but that the solubility of a different protein of interest, the Ad2 protein, was not as effected by the same vector sequences and further stated that “optimization of Ad2 knob solubility through mutagenesis approaches could provide insights into intrinsic factors that regulate protein folding and multimerization in vivo (page 1397, right column, paragraph 2).

Absent evidence to the contrary, one would have a reasonable expectation of success combining the teachings of the art because Freimuth et al showed that the substitution of various length peptide extensions into expression vectors was successfully practiced at the time Freimuth et al and Cordon et al were published.

In view of the foregoing, the vector of claim 64, as a whole, would have been obvious to one of ordinary skill in the art at the time the invention was made. Therefore, the claims are properly rejected under 35 USC §103(a).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Catherine S. Hibbert, Ph.D., whose telephone number is (571)270-3053. The examiner can normally be reached on M-F 8AM-5PM, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Weitach, Ph.D., can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Respectfully submitted,

Catherine S. Hibbert
Examiner/AU1636

/David Guzo/
Primary Examiner
Art Unit 1636